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LARGEST MULTI-CENTRE EVALUATION OF RADIOEMBOLISATION USING SIR-SPHERES FOR PATIENTS WITH INOPERABLE PRIMARY LIVER CANCER PUBLISHED IN *HEPATOLOGY*

***ENRY Evaluation in 325 Patients Affirms Efficacy and Safety of
Radioembolisation in Seriously-ill Patients and
Identifies Specific Populations who may Benefit from Treatment***

Pamplona, Spain (7 July 2011) – Results of the multi-centre European Network on Radioembolisation with Yttrium-90 Resin Microspheres (ENRY) analysis of the long-term outcomes related to survival and safety of radioembolisation using SIR-Spheres in patients with inoperable primary liver tumours were published on-line today in *Hepatology*, the peer-reviewed journal of the American Association of the Study of Liver Diseases.¹

Evaluation of 325 patients with inoperable primary liver cancer (unresectable hepatocellular carcinoma), who were treated by teams of liver specialists, oncologists, interventional radiologists and nuclear medicine physicians at eight centres in Germany, Italy and Spain, provided “robust evidence of the survival outcomes achieved with radioembolisation, including patients with advanced disease and few treatment options,” said Bruno Sangro, MD, PhD, Professor of Hepatology in the Liver Unit of the Clinical University of Navarra, Pamplona, Spain, and chair of the ENRY group.

About Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) occurs in people whose livers have become severely damaged or cirrhotic, due to conditions such as hepatitis and alcoholism. It is one of the ten most-common cancers in the world, with nearly 750,000 cases diagnosed annually, and the third-leading cause of cancer deaths.² It occurs with greatest frequency in regions where hepatitis is most often diagnosed, such as in Asia Pacific and Southern Europe.

Hepatocellular cancer can be cured only by surgery, either by resecting the diseased parts of the liver, or by transplantation with a liver from a healthy donor. These interventions, however, are inappropriate for the great majority of patients, whose survival may range from a few months to two or more years depending largely on the state of their liver at the time of their diagnosis and the extent of tumour invasion.

Findings of the ENRY Evaluation

The majority of the patients (82.5%) evaluated by the ENRY group had liver disease that was reasonably-well compensated (Child-Pugh class A), with underlying

cirrhosis (78.5%) and good ECOG Performance status (ECOG 0-1: 87.7%). However, many of them had multiple tumour nodes (75.9%), with disease present in both lobes of the liver (53.1%) and/or occlusion of the portal vein (the vessel that transports blood from the gastrointestinal tract to the liver) in either a branch of the vein (13.5%) or the main vessel (9.8%).

Over 40 per cent of the patients (41.5%) had progressed following one or more other treatments prior to receiving radioembolisation with SIR-Spheres (yttrium-90 resin microspheres; Sirtex Medical Limited, Sydney, Australia), including surgery or liver transplantation, percutaneous procedures such as ethanol injection or radiofrequency ablation of individual liver tumours, or vascular procedures such as transarterial embolisation (TAE) or chemoembolisation (TACE) that block the liver arteries that feed tumours.

Using Barcelona Clinic Liver Cancer (BCLC) staging criteria, the vast majority of patients evaluated by the ENRY group had either advanced (BCLC C: 56.3%) or intermediate (BCLC B: 26.8%) disease.

The patients who received radioembolisation (also called selective internal radiation therapy or SIRT) were administered a median dose of 1.6 GBq of beta-radiating yttrium-90 resin microspheres, predominately as a single procedure delivered transarterially to the liver via a catheter through the femoral and hepatic arteries. The median overall survival of the SIRT-treated patients evaluated by the ENRY group was 12.8 months. Survival varied significantly by disease stage: 24.4 months for patients in BCLC A; 16.9 months in BCLC B; and 10.0 months in BCLC C.

“As ENRY was not a prospective study, our findings must be interpreted conservatively,” Professor Sangro explained. “What we can say, based on our evaluation of a broad range of patients with HCC treated in routine clinical practice, is that radioembolisation using SIR-Spheres directly targets tumours and spares viable liver tissue, which enables us to reduce the burden of disease and potentially increase both the patient’s survival and quality of life. The greatest survival benefit can be expected in those patients with better performance status, fewer tumour nodules and no occlusion of the portal vein.

“It is also clear from our analysis,” he added, “that radioembolisation may be particularly helpful in four specific patient populations. These include, firstly, patients who might otherwise be considered for TACE but may benefit more from SIR-Spheres; patients who are poor candidates for TACE due to the high number of tumour nodules (>5) or spread to both lobes of the liver; patients who have previously failed TACE; and, finally, patients who are ineligible for TACE because of portal vein occlusion. These patients have few other treatment options.”

Other treatment options that have been demonstrated to extend survival for patients with inoperable HCC include TACE, which requires repeated interventional procedures and hospitalisation due to the resulting post-embolisation syndrome; and sorafenib, an oral medication taken twice daily which can give side effects leading to discontinuation of the drug in more than a third of patients (38%).³

The ENRY collaboration found that radioembolisation was very well-tolerated by these otherwise ill patients. More than half (54.5%) experienced fatigue; around one third (32.0%) reported nausea or vomiting; while slightly more than a quarter (27.1%) reported abdominal pain and one in ten reported a mild fever. These symptoms were transient in all cases.

A very small number of patients (3.7%) suffered from gastrointestinal ulceration, which can occur when some microspheres inadvertently pass into a gastric artery.

“Based on the ENRY evaluation,” Prof Sangro concluded, “we believe that radioembolisation merits routine use in a number of patients with primary liver cancer. Radioembolisation may also be a synergistic option when combined with newer pharmaceutical treatments, such as the tyrosine kinase inhibitor, sorafenib.”

Physicians and patients interested in participating in either of two recently-initiated randomised controlled trials of radioembolisation using SIR-Spheres may learn more at:

- www.soramic.de – the SORAMIC trial (www.clinicaltrials.gov identifier NCT01126645) is being conducted in Europe on SIR-Spheres combined with sorafenib compared to sorafenib alone in patients with HCC;
- www.sirvenib.com – the SIRveNIB trial (www.clinicaltrials.gov identifier NCT01135056) is being conducted in Asia Pacific and is comparing SIR-Spheres to sorafenib in patients with HCC.

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For Further Information:

SIR-Spheres are approved for use in Australia, the European Union (CE Mark), New Zealand, Switzerland, Turkey and several other countries for the treatment of unresectable liver tumours.

SIR-Spheres are also fully FDA-approved and are indicated in the U.S. for the treatment of non-resectable metastatic liver tumours from primary colorectal cancer in combination with intra-hepatic artery chemotherapy using floxuridine

Downloadable images, media background information, a mode of action video and further supporting materials are available online at www.SIRTnewsroom.com.

References:

1. Sangro B, Carpanese L, Cianni R *et al* on behalf of European Network on Radioembolization with Yttrium-90 resin microspheres (ENRY). Survival after ⁹⁰Y resin microsphere radioembolization of hepatocellular carcinoma across BCLC stages: A European evaluation. *Hepatology* 2011; ePub doi: 10.1002/hep.24451.
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3. Llovet J, Ricci S, Mazzaferro V *et al* for the SHARP Investigators Study Group. Sorafenib in advanced hepatocellular carcinoma. *New England Journal of Medicine* 2008; **359**: 378–390.

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